Antibiotic treatment of suspected neonatal meningitis

Sir,—The annotation on antibiotic treatment of suspected neonatal meningitis seems to demonstrate that optimal treatment of this thankfully rare disorder is still not clear. The suggested array of antibiotic treatment and combined routes of administration may provide cover against a wide range of organisms, but is such treatment in the best interests of every patient? In a sick hypotensive infant who may already have compromised renal function the combination of aminoglycoside and cephalosporin may exacerbate the problem. To state that 'Gentamicin should be used primarily to treat the associated septicaemia' and 'Interleukin-1 concentrations in the cerebrospinal fluid correlate well with the degree of meningeal inflammation and with the outcome.' Ventricular cerebrospinal fluid samples from the 1970s study performed by McCracken and his colleagues were stored in the deep freeze at the time, and their endotoxin and cytokine concentrations have recently been examined by Mustafa et al (1989). They found increased endotoxin and very much higher interleukin-1 concentrations in the cerebrospinal fluid of the group treated with intraventricular antibiotics than in those only treated intravenously. Endotoxin concentrations of 78 mg/ml in the intraventricular group compared with 22 mg/ml in those given intravenous treatment alone. Similarly, mean interleukin-1 concentrations as high as 5024 pg/ml in the patients given gentamicin contrasted with mean concentrations of 87 pg/ml in patients treated with intravenous antibiotics alone. This effect is likely to be due to bacterial lysis, releasing endotoxin and other bacterial cell wall products by very high local concentrations of intraventricular gentamicin. The resulting cytokine production would appreciably exacerbate the inflammatory response within the ventricles. Thus, although intraventricular antibiotics may be appropriate treatment in neonatal meningitis (although there is little firm evidence either way), it is important to modulate the resultant inflammatory response as well as to kill the bacteria. Considerable recent work, particularly from McCracken's group, has shown that dexamethasone can do this both in the experimental animal and in juvenile animals with meningitis. Until we recognise that the treatment of meningitis should include the suppression of excessive inflammation as well as the destruction of the pathogen we are unlikely to improve the prognosis in this serious and distressing disease.  


Dr Rennie and Gandy comment: Thank you for giving us the opportunity to reply to the correspondent regarding editorial. Opinions regarding the benefits of intraventricular treatment in neonatal Gram negative meningitis are likely to continue to differ for some time; our recommendations concerning meningitis and the other infective conditions are mediated through the release of cytokines, particularly tumour necrosis factor and interleukin-1, from cells after their exposure to bacterial endotoxin and other cell wall material. Interleukin-1 concentrations in the cerebrospinal fluid correlate well with the degree of meningeal inflammation and with the outcome. Ventricular cerebrospinal fluid samples from the 1970s study performed by McCracken and his colleagues were stored in the deep freeze at the time, and their endotoxin and cytokine concentrations have recently been examined by Mustafa et al (1989). They found increased endotoxin and very much higher interleukin-1 concentrations in the cerebrospinal fluid of the group treated with intraventricular antibiotics than in those only treated intravenously. Endotoxin concentrations of 78 mg/ml in the intraventricular group compared with 22 mg/ml in those given intravenous treatment alone. Similarly, mean interleukin-1 concentrations as high as 5024 pg/ml in the patients given gentamicin contrasted with mean concentrations of 87 pg/ml in patients treated with intravenous antibiotics alone. This effect is likely to be due to bacterial lysis, releasing endotoxin and other bacterial cell wall products by very high local concentrations of intraventricular gentamicin. The resulting cytokine production would appreciably exacerbate the inflammatory response within the ventricles. Thus, although intraventricular antibiotics may be appropriate treatment in neonatal meningitis (although there is little firm evidence either way), it is important to modulate the resultant inflammatory response as well as to kill the bacteria. Considerable recent work, particularly from McCracken's group, has shown that dexamethasone can do this both in the experimental animal and in juvenile animals with meningitis. Until we recognise that the treatment of meningitis should include the suppression of excessive inflammation as well as the destruction of the pathogen we are unlikely to improve the prognosis in this serious and distressing disease.

come to reconsider the 1970 European Society of Paediatric Gastroenterology and Nutrition (ESPGAN) diagnostic criteria for gluten sensitive enteropathy, we do not entirely agree with the timing of the diagnostic intestinal biopsy proposed by our Italian Group of Paediatric Gastroenterology at the meeting in Trieste, May 1987, and recently published. A multicentre study indicates that in Italy the vast majority of diagnoses of gluten sensitive enteropathy (more than 90%) are made in young children who are referred with signs of malabsorption and are then found positive for the antigliadin antibody test. At the Trieste conference it was stated that these so called typical cases do not need a gluten challenge and can be readily and definitely diagnosed by a single biopsy specimen showing a flat mucosa at the first work up.

Looking back on our hundreds of biopsies we have noticed that whenever the clinical and laboratory data strongly suggested gluten sensitive enteropathy, we nearly always found a flat mucosa at the first intestinal biopsy. It appears then that the initial biopsy recommended by ESPGAN and retained by the Trieste recommendations is seldom informative as its result is highly predictable in typical patients. In these cases (supported by a positive antigliadin antibody test and abnormal intestinal permeability test) we suggest that the initial biopsy is avoided and a six to 12 month period of gluten free diet is commenced (figure).

As the first years of a gluten free diet seem to have an imprinting effect on the long term compliance, we believe that the gluten challenge is, at present, unavoidable in the youngest patients because it demonstrates the persistence of, or the degree to, the patient’s family. At the end of a three to six month period of gluten challenge (or less if symptoms develop) a biopsy is highly recommended as the relapse is sometimes evident only at the histological level. This single biopsy specimen will confirm the diagnosis of gluten sensitive enteropathy in most cases. If the mucosa looks normal the patient can be left on a free diet and periodically checked to exclude the possibility of a late response to gluten. In our opinion a short period of gluten ingestion, as we propose, should not expose the patient to significant risks.

The above approach is less invasive than the ESPGAN scheme and fully exploits the diagnostic role of the antigliadin antibody test at the first assessment of the patient. We also suggest adding the sugar intestinal permeability test, which has proved to be a reliable screening procedure for gluten sensitive enteropathy. For atypical or late onset cases we agree that an intestinal biopsy is always mandatory during the first diagnostic phase. A conclusive note of caution is needed. It is well known that long term treatment of gluten sensitive enteropathy is often unsatisfactory. This is especially true for patients who have found 'sensitive' doctors who are overzealous in their wish to avoid unpleasant biopsies. So far we have followed the ESPGAN diagnostic criteria for coeliac disease with satisfactory results both for patients and for us. Nevertheless, in the light of the new, non-invasive diagnostic tools, we also agree on the need of revising the ESPGAN recommendations. This attempt should be made with the contribution of experts from several European centres.

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Urinary growth hormone excretion

Sir,—The paper by Walker and colleagues on the use of urinary growth hormone excretion as a screening test for growth hormone deficiency, Arch Dis Child 1990;65:89-92.

Urinary growth hormone excretion


Pulse 1990 January 20:3.

Dr Walker comments: The value of a non-invasive test of growth hormone secretion in children would be immense. Although of considerable promise, the study of Walker and colleagues does not yet justify the general introduction of urinary growth hormone estimations and more validation is necessary to establish the full characteristics of this potentially valuable addition to our range of investigations.


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